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Breathing of half-micron aerosols I. Experimental

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DAVIES, C. N., J. HEYDER, AND M. C. SUBBA RAMU. *Breathing of half-micron aerosols. I. Experimental.* J. Appl. Physiol. 32(5): 591–600. 1972.—The breathing of 0.5-μ-diameter aerosol particles by man has been studied from continuous records of volume and concentration. During steady breathing at a constant tidal volume the deposition of particles in the lungs increases as the expiratory reserve volume (ERV) decreases and can be expressed as a function of the difference between the ERV adopted when measuring deposition and the subjects' normal ERV. After steady breathing of aerosol the end-reserve concentration is always finite. After a single breath it is zero, provided that the lungs were operating above the normal ERV. If the lungs are deflated to a low breathing level a finite end-reserve concentration is found. Even when the end-reserve concentration is zero, some aerosol remains behind in the lungs. Experiments on the washin of aerosol show that steady breathing conditions are nearly established after four breaths. Washout experiments prove that particles remain airborne in the lungs during nine breaths. Recoveries of aerosol were measured in tidal air and reserve air after a single breath and are related to the recoveries after steady breathing.

particles; inhalation of aerosol; deposition of aerosol; ERV and aerosol deposition

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AEROSOLS of quite uniform particles, the geometrical standard deviation being 1.15 on a mean diameter of 0.5 μ, have been produced from di(2-ethylhexyl)sebacate of density 0.91 g/cm^3 condensed upon nuclei of sodium chloride. They are harmless to breathe and the particles evaporate so slowly as not to matter. Using a specially sensitive method of recording continuously the inhaled and exhaled concentrations, Muir and Davies (7) measured the deposition of aerosol (relative deposition, D, is equal to one minus the fraction of the aerosol breathed in which was recovered when breathed out). The results for steady breathing, averaged over 10 or more breaths after the wash in breaths had been completed, were expressed by Davies (4) as a function of tidal volume (V_T, cm^3) and frequency of breathing (F, cycles/min) in the following expression:

$$100\,D = 16.5 + V_T/400 - 2\sqrt{F} \qquad (1)$$

for the ranges $400 < V_T < 2{,}200$ cm^3, $10 < F < 30$ cycles/min. The relationship of these results to earlier work was also discussed (4, 7).

There was a good deal of scatter in the experimental results, covering a range of some $\pm 30\%$ of the mean value of D in the worst cases, but it was noticed that the scatter diminished as the tidal volume increased. When breathing with a large tidal volume the resting expiratory level is subject to less arbitrary variation than it is for shallow breathing (Fig. 1); a variation of D with the resting expiratory level, or expiratory reserve volume, was therefore suspected and experiments were carried out to study the effects of accidental and deliberate changes of breathing level (see DEFINING THE RESTING EXPIRATORY LEVEL).

EXPERIMENTAL APPARATUS

The apparatus consists of a homogeneous aerosol generator and a storage box that is filled with aerosol at the beginning of an experiment. As the subject consumes aerosol he exhales into a balloon, inside the box, so that there is no dilution or change of pressure. Inhaled and exhaled concentrations are recorded continuously alongside a spirometer record of air volume. The aerosol particles pass through a measuring cell, very close to the subject's lips or nose.

The apparatus of Muir and Davies (7) was improved for the present series of experiments. A quartz-halogen lamp now illuminates the aerosol particles in the center of the measuring cell and the light that they scatter at right angles is collected by a more sensitive photomultiplier. The aerosol chamber, containing the balloon into which the subject exhales via a spirometer, is kept near to lung temperature and humidity. Warm water circulates from a tank through the measuring head and the spirometer; the tank contains a coil of pipe through which filtered air is drawn into the apparatus. A second chamber, also containing a balloon, is now provided and maintained near body temperature and humidity; at the commencement of an experiment this is filled with filtered air so that the subject can change from air to aerosol at any time without losing the spirometer record. The circuit of the breathing apparatus is shown in Fig. 2.

It was felt necessary to construct an artificial device of standard performance so that the functioning of the rather complicated apparatus could frequently be verified; the device consisted of a breathing machine with a tidal volume of 250 cm^3 operating at 18.5 breaths/min; the machine was attached to an artificial lung which fitted directly on to the mouthpiece used by human subjects. The artificial lung consisted of a U tube (1.7 cm internal diameter, total length of 35 cm) filled with glass spheres 0.45 cm in diameter; it was immersed in a jacket in the warm-water circuit. The deposition of 0.5-μ-diameter aerosol particles in this device, during steady breathing, was 0.434 ± 0.016 (20 observations spread over the period of all the human experiments).

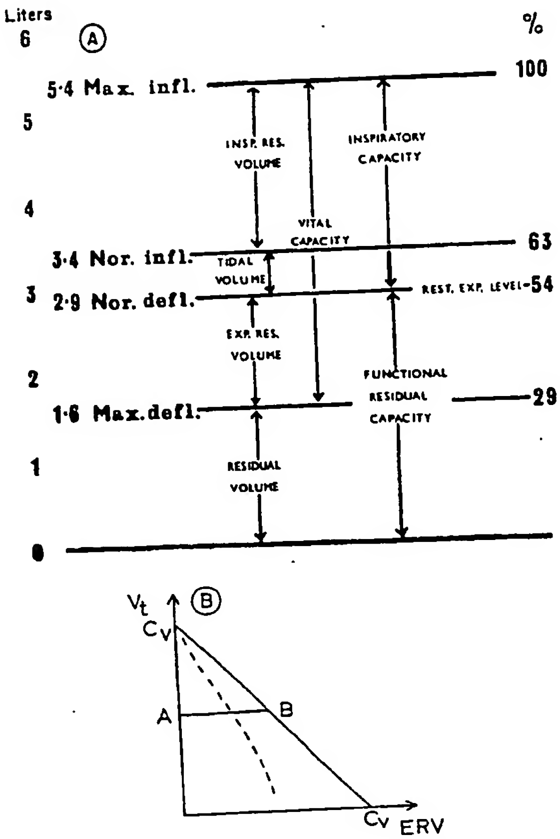

FIG. 1. *A:* subdivisions of lung volume after Aslett et al. (2). *B:* range AB of expiratory reserve volume (ERV), or the value of the resting respiratory level, is liable to less arbitrary variation in subjects breathing at a large tidal volume (VT).

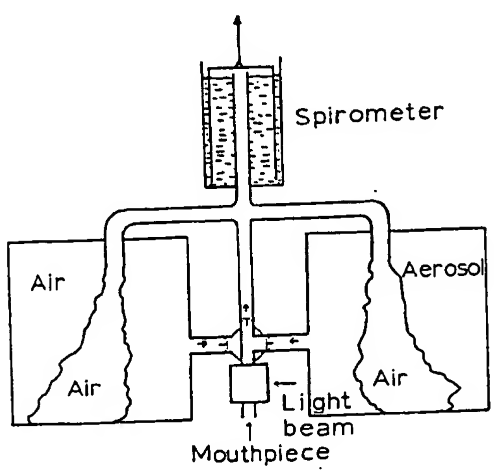

FIG. 2. Aerosol breathing apparatus.

EXPERIMENTAL METHOD AND CORRECTIONS

The subject breathes aerosol in time with a metronome and watches a pointer attached to a light spirometer bell, the movement of which is recorded alongside the record of aerosol concentration.

The actual amount of aerosol inhaled or exhaled can thus be calculated as a function of time while the subject controls his tidal volume, as well as he can, and is able to change his resting expiratory level by watching the movement of the pointer while he is breathing.

It was found that even experienced subjects inhaled and exhaled unequal volumes in a given breath. The difference could be made negligible by a really careful, trained subject but ordinary persons often had differences exceeding 10% of the tidal volume. Clearly, if a greater volume is inhaled the amount of aerosol left in the lungs, after exhaling a lesser volume will be too large and the uncorrected deposition for that breath will be high. Conversely, if more aerosol is exhaled than inhaled the deposition for that breath is below average. These differences increase the scatter of calculated deposition from breath to breath and do not always average out over 10 breaths.

There is also the question of instrumental dead space. The subject breathes while holding in his mouth a short, wide tube that is connected to the measuring cell. The latter is traversed by a narrow pencil of intense light, which is scattered by the particles in the center of the cell; some of the scattered light is recorded. The light beam is about 4 cm from the lips and the total volume of the cell, between the lips and the three poppet valves that control the inlet of air or aerosol and the outlet, is 40 cm³. Not more than 11 cm³ of this volume was between the light beam and the lips. During exhalation, the recorded trace of concentration falls steeply to the end-exhalation value and then climbs rapidly as soon as inhalation of new aerosol commences. A small volume of aerosol near the light beam is therefore at end-exhalation concentration at the beginning of inhalation and the trace of concentration is nearly linear from the instant when inhaling starts up to the attainment of full concentration about 0.24 sec later (see Figs. 3 and 5). In calculating their results, Muir and Davies (7) assumed that the concentration was equal to the end-tidal value in the whole 40 cm³ of instrumental dead space. In the present work the mean of the end-tidal value (C_1) and the full inhaled value (Ci) was taken over the volume up to the attainment of C_1 which was usually rather less than 40 cm³, since this was in close agreement with the records and it has been found that the response of the recorder was virtually instantaneous.

To see how this correction affects the results, an example is considered where the tidal volume is 600 cm³ and the correct deposition is 0.105. The concentration at end exhalation is 0.65 Ci. The values are given in Table 1; as a rule, the correction was smaller than this.

TABLE 1. *Old and new methods of correcting for instrumental dead space*

Dead-Space Concn	Amount of Aerosol Inhaled	Amount of Aerosol Exhaled	Deposition Calc
0.65 Ci (assumed)	560 Ci + 40 × 0.65 Ci = 586 Ci	531 Ci	$1 - \frac{531}{586} = 0.094$
½ (0.65 + 1.0) Ci (based on linear rise on commencing to inhale)	560 Ci + 40 × 0.83 Ci = 593 Ci	531 Ci	$1 - \frac{531}{593} = 0.105$

The deposition in this example is thus 11% low when calculated on the assumption of the end-exhaled aerosol occupying the entire instrumental dead space. This correction is not of great importance in steady breathing since subject differences are greater. It is, however, necessary to allow correctly for the dead space in the interpretation of some single-breath experiments to be discussed later.

The corrections for unequal volume and instrumental dead space during steady breathing are illustrated in Fig. 3 which shows the concentration and volume records which are obtained and integrated graphically.

Let D'_u be the uncorrected fractional deposition, then

$$D'_u = 1 - \int_0^{Ve} Ce\, dV/ViCi \qquad (2)$$

where Vi is the volume inhaled, Ve the volume exhaled, Ce the variable concentration exhaled, and Ci the constant (apart from instrumental dead-space) concentration inhaled.

Correcting for the instrumental dead space of 40 cm^3 defines D_u where

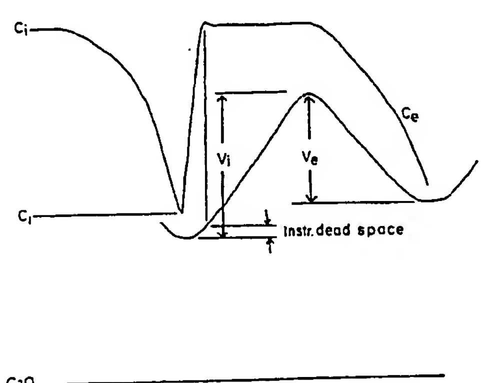

FIG. 3. Recording of concentration of aerosol (C) and volume of aerosol (V) showing instrumental dead space and unequal inhaled nd exhaled volumes.

$$D_u \doteq 1 - \int_0^{Ve} Ce\, dV \Big/ \cdot \{Ci(Vi - 40) + (1/2)40(Ci + C_1)\} \qquad (3)$$

C_1 is the concentration at end exhalation of the preceding breath.

If Vi and Ve are not equal a correction is required to the amount of aerosol inhaled so that it is equal to the volume exhaled. This gives the final, corrected deposition as

$$D_o = 1 - \int_0^{Ve} Ce\, dV \Big/ \cdot \{Ci(Vi - 40) + (1/2)40(Ci + C_1) + Ci(Ve - Vi)\} \qquad (4)$$

The correction $|D_u - D_o|$ never exceeded 15% and was given by

$$(D_u - D_o)\ \% = -0.146\ (Ve - Vi) \qquad (5)$$

the volumes being in cubic centimeters.

The standard deviation of the values of deposition calculated from successive breaths during steady breathing was reduced from 0.0383 to 0.0180 over a series of experiments with four subjects and a total of about 140 breaths; the mean corrected deposition was 0.117 ± 0.018 at a mean tidal volume of 630 cm^3 and a mean frequency of 16.5 breaths/min. This value is 17% higher than the value (0.100) given by *equation 1.* Some of this difference is due to the improved method now used to correct for the instrumental dead space. The standard deviation includes subject and breathing level differences which are discussed below.

DEFINING THE RESTING EXPIRATORY LEVEL

It was felt that some of the differences between steady deposition for different observers and between the same observer's results on different occasions might be due to changes in the resting expiratory level. To test this idea a dozen experiments were carried out with three subjects in which breathing the aerosol first took place normally. The observer then deflated his lungs by some 600–800 cm^3

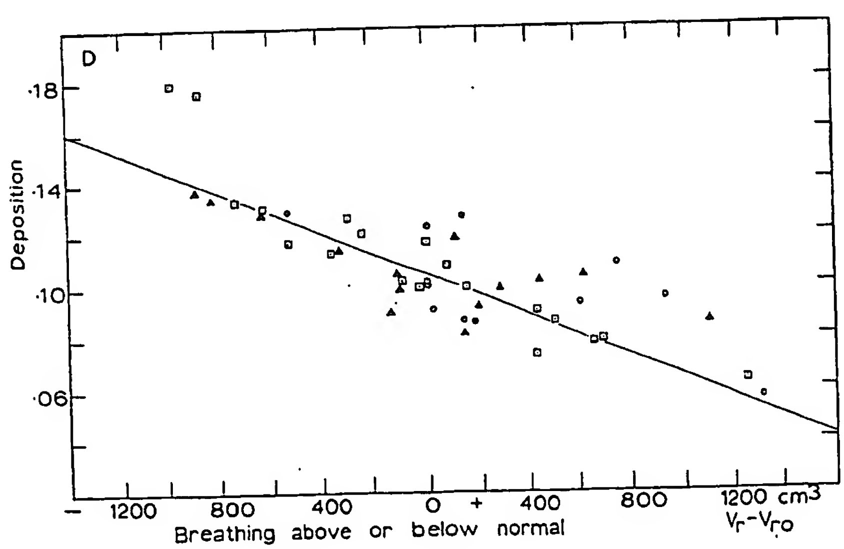

FIG. 4. Deposition of 0.5-μ aerosol during steady breathing at 16 cycles/min with a tidal volume of 600 cm^3. Vr_0 = normal expiratory reserve volume of subject; Vr = experimental value. For normal expansion of lungs $Vr - Vr_0 = 0$; underexpansion, positive values to the right. ○, *Subj CND;* △, *subj JH;* ◻, *MSR;* ——— *equation 6.*

TABLE 2. *Steady breathing of 0.5-μ aerosol*

Subject, Vr_0	Vr, cm³	Vt, cm³	D	F, breaths/min	Final Concn at End of Deep Exhalation/Inhaled Concn	Recovered Fraction of Amount of Aerosol Inhaled in Last Breath	
						In tidal air	In reserve air
CND, 835 cm³	835	620	0.123	16.2			
	835	661	0.013	17.1			
	835	632	0.102	17.0			
	936	579	0.126	16.7			
	1,012	580	0.085	16.9			
	2,150	500	0.053	17.1			
	1,760	508	0.093	16.9			
	1,445	517	0.091	16.9			
	972	379	0.086	15.5	0.040	0.916	0.326
	835	598	0.091	16.5	0.034	0.911	0.366
	1,587	593	0.108	15.8			
	287	488	0.126	15.8		0.857	0.161
JH, 1225 cm³	900	620	0.114	16.8	0.028	0.903	0.287
	1,125	664	0.109	17.0			
	1,360	620	0.087	18.0	0.016	0.932	0.310
	1,500	610	0.104	18.0	0.016	0.889	0.289
	1,220	556	0.100	15.7	0.021	0.911	0.311
	1,130	552	0.098	15.8	0.041	0.959	0.404
	1,930	602	0.120	16.5	0.009	0.920	0.281
	1,419	583	0.094	16.8	0.022	0.922	0.318
	400	643	0.135	16.3			
	2,325	640	0.087	16.2			
	1,063	623	0.092	16.5			
	1,850	638	0.105	16.2			
	341	572	0.136	15.9			
	590	615	0.128	15.8			
	1,668	537	0.099	15.6			
MCS, 1040 cm³	1,733	530	0.078	16.0			
	1,040	500	0.114	16.0			
	404	697	0.129	17.0			
	1,470	675	0.090	16.8			
	960	632	0.099	17.0			
	971	589	0.083	16.8	0.042		
	687	713	0.111	16.6			
	1,110	724	0.111	15.5			
	1,465	715	0.070	15.8			
	1,700	700	0.069	15.0			
	303	694	0.133	16.6	0.075		
	1,182	678	0.100	16.8	0.030		
	507	709	0.117	17.2			
	755	720	0.125	16.2			
	1,545	730	0.086	16.2			
	61	689	0.175	16.2			
	168	694	0.176	15.6			
	809	681	0.114	15.6			
	2,291	602	0.063	15.8			

TABLE 3. *Measurements of normal expiratory reserve volume*

Observers	Spontaneous Variations of Expiratory Reserve Volume,* cm³	No. of Observations	Corresponding Changes in Deposition†
CND	835 ± 180	10	± 7% △
JH	1,225 ± 204	20	± 8% ⊙
MCS	1,040 ± 330	10	± 12% ⊡

* Values are means ± SD. † According to *equation 6* within limits of SD in column 2.

and breathed another series of nearly identical breaths at the lower level. Finally he expanded to 600–800 cm³ above the initial, normal level and performed a third series at the higher level.

These experiments showed clearly that the deposition decreased when the resting expiratory level was raised. Since, however, there was still no check on the expiratory reserve volume a different procedure was adopted. The observer arranged his lung volume at a predetermined level and carried out the breathing of aerosol at this level. After 10 or so breaths he then made a maximal deflation which was recorded. The resting expiratory level during the breathing of aerosol was therefore known in relation to maximal deflation.

The results of these experiments, for three subjects, are shown on Fig. 4 and in Table 2. During the experiments the range of tidal volume was from 490 to 730 cm³ and of frequency from 15.5 to 18.0 cycles/min; the experimental points on the graph have all been corrected to 600 cm³ and 16 cycles/min by *equation 1*. The straight line shown on the graph has the equation

$$100\,D = 17.0 + V_T/400 - 2\sqrt{F} - \frac{2}{500}(V_r - V_{r_0}) \qquad (6)$$

with $V_T = 600$ cm³ and $F = 16$ cycles/min; V_{r_0} is the normal expiratory reserve volume of the subject and V_r the value adopted during the experiments for which $60 < V_r < 2{,}400$ cm³. Each symbol relates to a different subject. It will be seen that there is an indication, with one subject, that a departure from the linear relationship of *equation 6* occurs for $V_r < 200$ cm³ with high deposition at very low reserve volumes. Another observer shows a departure at high reserve volumes, the deposition being nearly constant for $V_r > 1{,}500$ cm³.

To measure the normal expiratory reserve volume V_{r_0} and to find out how much it was likely to vary from one occasion to another, the volume of each subject was measured repeatedly once a day; the subject simply sat at the apparatus, relaxed, breathed, and exhaled into it with no attempt at previous adjustment of his breathing level. The results are shown in Table 3: the last column shows the range of measured deposition which may be expected if the subject adopts an arbitrary breathing level within the range of the standard deviation given in column 2.

It is clear that a large part of the scatter in deposition calculated from experiments in which aerosol has been breathed can be due to arbitrary changes in the expiratory reserve volumes of the subjects and to differences between the normal volumes of different subjects.

It has been noted by Briscoe (3) that measurements of functional residual capacity are much more variable than those of vital capacity. The latter does not depend on breathing level. Just as the arbitrary choice by a subject of expiratory reserve volume (ERV) is reflected in his aerosol deposition so, as is clear from Fig. 1*A*, must it also govern his measured functional residual capacity; this is not, however, stated in the text quoted.

When experimental measurements depend on breathing level, but no attempt is made to control it, the scatter is likely to be less when the tidal volume is large. The reason for this can be seen from Fig. 1*B*. Consider two limiting conditions: *a*) when V_T tends to zero, the ERV can, in principal, take any value between zero and the vital capacity (VC); and *b*) when the ERV tends to zero, V_T can take any value between zero and the VC.

The range of V_T covered in a series of experiments might

be related to the ERV by some line such as that shown broken in Fig. 1*B*. The particular value of the ERV associated with a given value of V_T is liable to spontaneous variation when the experiments are repeated. It is clear that the range available to the ERV at a particular value of V_T, as indicated by the line AB, becomes less when V_T is greater. Arbitrary changes in the ERV during breathing experiments will thus have less effect on quantities such as functional residual capacity and aerosol deposition when the tidal volume is large.

WASHIN AND WASHOUT OF AEROSOL WHEN BREATHING STEADILY

A record showing the changeover from breathing air to aerosol is shown in Fig. 5*A*. The transfer was made at end exhalation; the concentration of aerosol rises rapidly from zero to Ci while the instrumental dead space fills during the first 0.24 sec of the first inhalation of aerosol. During the completion of inhalation the concentration is constant; then, on breathing out, it falls to the end-exhalation value. This value is small for the first breath of aerosol and rises with succeeding breaths until after the fourth it fluctuates about the average value for steady breathing of aerosol. Washin is complete, as far as external indications go, by the end of the fourth breath of aerosol. The discussion in this section relates to tidal volumes of about 600 cm³ and frequencies near to 16 breaths/min.

On return to clean air, as shown on Fig. 5*B*, after having breathed aerosol for 14 or more breaths, the concentration during the first breath of air drops to zero when the instrumental dead space has been washed out. It remains zero during the completion of inhalation and for a part of exhalation; the concentration then rises slowly at first, until exhalation is complete, there being no fall in concentration during the exhalation of one tidal volume. The delay in the appearance of aerosol increases and the amount of aerosol washed-out decreases, breath by breath.

In place of deposition it is more appropriate to discuss washin and washout in terms of the recovery of aerosol by exhaling. Deposition is easy to define only during steady breathing. Since there is a steady loss of particles during breathing over a period, it is evident that deposition is taking place in the lungs and can be measured by comparing the quantities of particles which are inhaled and exhaled. It will be seen that the deposition of 0.5-μ particles inhaled during a given breath does not take place during that breath but is delayed and then continues over the duration of a number of breaths. During the transient conditions of washin and washout it is therefore incorrect to refer to the disappearance of particles from a particular breath as deposition.

If I_n is the amount of aerosol inhaled in the nth breath of aerosol washin after breathing air and E_n is the amount of aerosol exhaled in this breath, then the fractional recovery is

$$R_n = E_n/I_n \qquad (7)$$

During steady breathing the fraction recovered is R, which is, in principle, the same for each breath and is related to the fractional deposition, D, as follows:

$$D = 1 - R \qquad (8)$$

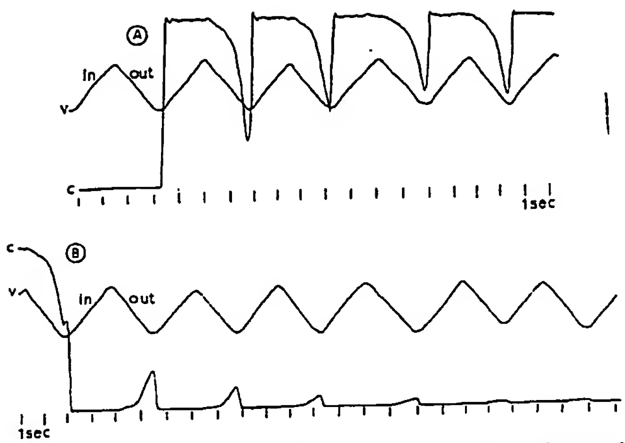

FIG. 5. Records of concentration of aerosol (C) and volume of aerosol inhaled or exhaled (V). *A:* washin; *B:* washout.

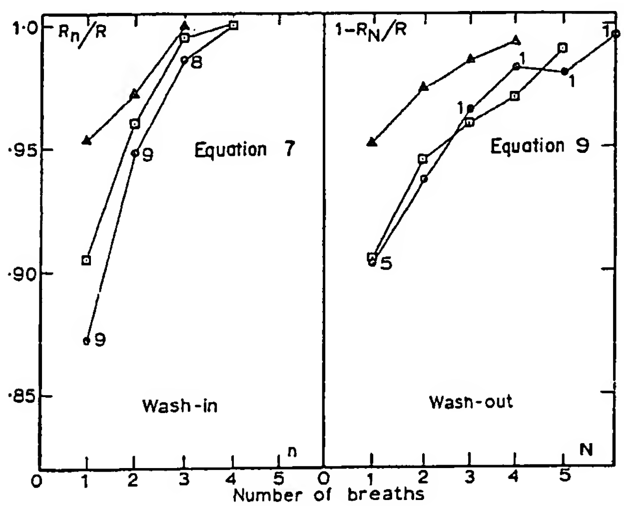

FIG. 6. Washin of aerosol during successive breaths (*eq 7*); washout of aerosol after steady breathing during N successive breaths of clean air (*eq 9*). ⊙, *Subj CND;* mean ERV 1,320 cm³; no. of separate experiments shown by each point. △, *Subj JH;* mean ERV 1,300 cm³; 7 experiments. ⊡, *Subj MSR;* mean ERV 1,200 cm³; 2 experiments. $\sum$R (*eq 9*).

Similarly, during washing out by breathing air after aerosol, suppose I_l is the amount of aerosol which was inhaled in the last breath of a sequence of steady breathing of aerosol. Then, putting E_N equal to the amount of aerosol exhaled in the Nth breath of air the recovery during washout is

$$R_N = E_N/I_l \qquad (9)$$

R_n/R rises from zero to unity during washin. During washing out, $1 - R_N/R$ rises from zero to unity. The value of R during steady breathing is about 0.9 and the standard deviation of individual experiments was about 15%, as described in EXPERIMENTAL METHOD AND CORRECTIONS. It was therefore impossible to distinguish between R_n and R beyond four breaths of washin. As far as can be told from the experimental plots on Fig. 6, washin was complete in four breaths.

In the case of washout R_N tends to zero and it was possi-

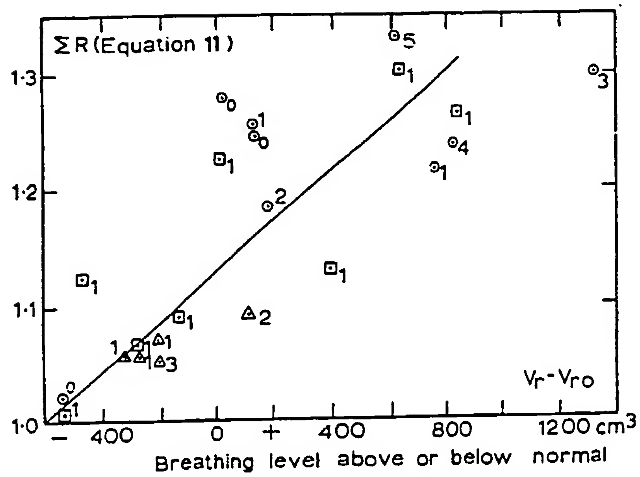

FIG. 7. Recovery of aerosol, after steady breathing, in zero to five breaths of clean air followed by a deep exhalation. Each point is the result of one experiment; no. of breaths of clean air is marked beside the points. ⊙, *Subj CND;* △, *subj JH;* ⊡, *subj MSR.* $\sum R$ (*eq 11*) is shown as a function of breathing level, $Vr - Vr_0$.

ble to detect the presence of only 1 % of aerosol against a background of zero concentration; it was thus possible to follow washout to six breaths as shown on Figs. 5*B* and 6, and sometimes to nine.

In the third paper of this series Heyder and Davies (5) show that a simple model for exchange of particles between tidal, reserve, and residual air, free from any assumptions about the mechanisms of exchange, makes it necessary for

$$R_n/R = 1 - R_N/R \qquad (10)$$

for n = N. The washin and washout curves of Fig. 6 do not coincide in this way; further experiments are needed to see if this is because of the experimental difficulty just referred to.

There is inevitably more scatter in the results for transient conditions of breathing than there is in the steady-state deposition values. During steady breathing each experiment provides 10 or more numbers that can be corrected, as described above, and averaged. For each observation during transient conditions, however, only a single value is obtained in a given experiment.

DEEP EXHALATION AFTER STEADY BREATHING OF 0.5-μ AEROSOL

Another method of recovering some of the aerosol that has been inhaled during steady breathing is to make a deep exhalation so that all the expiratory reserve air is breathed out and only the residual air remains in the lungs. During steady breathing a distribution of aerosol concentration becomes established throughout the lungs. The particles that are not recovered when a deep exhalation is made must either be in the residual air or deposited on the walls of the lungs.

A series of experiments was performed in which aerosol was first breathed steadily for some 20 breaths so as to establish the steady-state distribution of concentration. The experiments were varied by making the deep exhalation either at once or else after one, two, three, up to five breaths of clean air after ceasing to breathe aerosol. The idea was to allow time for some of the aerosol in the reserve air to transfer to the residual air and so to become irrecoverable.

In fact, no significant variation could be detected in the total amount of aerosol recovered, either from the deep exhalation of the last aerosol breath, or from the normal exhalation of the last aerosol breath plus the washout in one to five breaths of air, plus the deep exhalation of the last breath of air. The total recovery did not depend on the number (0–5) of breaths of clean air but lay within a band of ± 10 % which correlates well with the expiratory reserve volume; this volume was obtained, in every experiment, from the deep exhalation.

The exchange theory of Heyder and Davies (5) predicts a decrease in total recovery of only 11.4 % with five breaths of clean air intervening between the last tidal breath of aerosol and the exhalation of reserve air. It is therefore not surprising that no consistent decrease of recovery could be demonstrated over the experiments shown in Fig. 7.

Unlike recovery in a tidal exhalation the aerosol in a deep exhalation always shows a peak concentration. The concentration rises throughout the tidal part of the deep exhalation and reaches a peak near to the end-tidal volume. The rise in concentration to the peak is more rapid than the fall and the location of the peak is the same irrespective of the number of tidal washouts.

The results of these experiments are plotted on Fig. 7. The values are relative to the amount of aerosol inhaled in the last breath of aerosol, I_l. If N is the number of breaths of clean air, the total recovery in a particular experiment is

$$\left.\begin{aligned}\sum R &= E_d/I_l & N &= 0\\ &= (E_l + E_d)/I_l & N &= 1\\ &= (E_l + E_1 + E_d)/I_l & N &= 2\\ &\;\;\vdots & &\\ &= (E_l + E_1 + E_2 + E_3 + E_4 + E_d)/I_l & N &= 5\end{aligned}\right\} \qquad (11)$$

where E_l is the amount normally exhaled in the last breath of aerosol, E_d is the amount in the deep exhalation and E_1, E_2, . . . are the amounts exhaled in the first, second, . . . breaths of clean air.

The proportion of the total recovery, ΣR, which is found in the final, deep exhalation decreases from 1 (N = 0) to about 0.1 (N = 5); values for a given N depend on the expiratory reserve volume.

The fall in concentration in the exhaled air throughout the course of a deep exhalation is shown in Fig. 8. The curves were obtained immediately after the last normal tidal inhalation, of a series of 20 or so, with no breaths of clean air intervening. The tidal volume in all cases was near to 600 cm³ and the rates of inhalation and exhalation, and of the deep exhalation, were natural to a frequency of about 16 breaths/min.

Figure 9 and Table 2 show that the aerosol concentration, when the reserve air had been completely breathed out at the end of the deep exhalation, never reached zero, even when breathing took place at higher reserve volumes (up to 1.5 times normal); the final concentration increases as the reserve volume is decreased. Although both the value of the final concentration and the recovery of aerosol in

the deep exhalation correlate quite well with the expiratory reserve volume, there is not a lot of difference in the shape of the curves of Fig. 8. The end concentration must represent the concentration during steady breathing at the interface of reserve air and residual air. This is true after steady breathing when, throughout the whole of the lungs, a distribution of aerosol concentration will have become established; as will be seen below, it is not so in single-breath experiments because some alveolar regions then contain no particles at all and it is some of these which empty last, at the end of a deep exhalation, provided that the reserve volume is not too small.

SINGLE-BREATH EXPERIMENTS

In these experiments a tidal volume of about 600 cm³ of aerosol was inhaled after the lungs had been thoroughly washed out by breathing clean air at the same tidal volume and expiratory reserve level. Exhalation then took place, at the same rate as for steady breathing, to the end of the

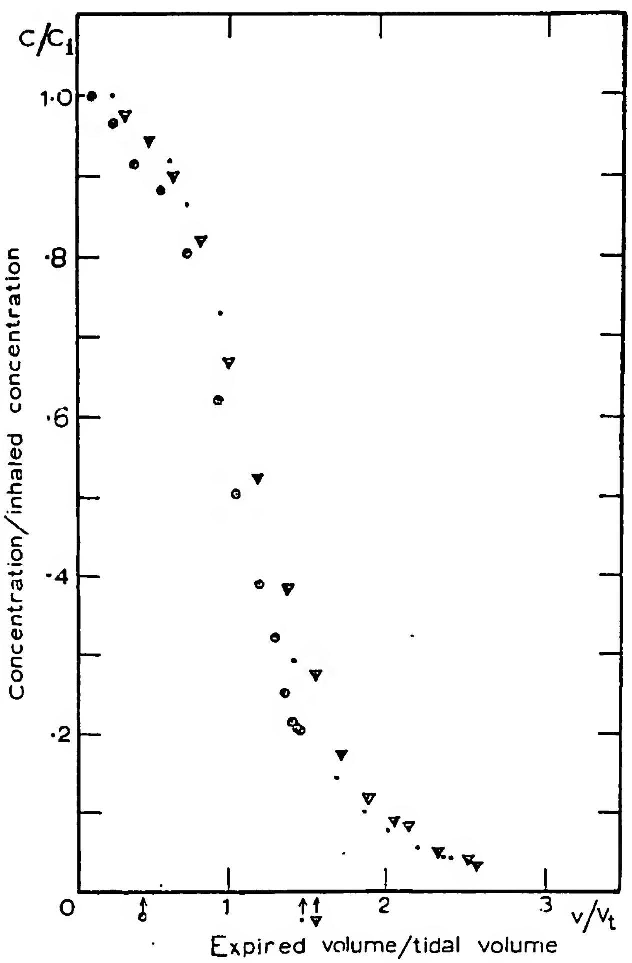

FIG. 8. Fall in concentration (C) of aerosol throughout a deep exhalation after steady breathing. Ci = inhaled concentration; V = volume exhaled; V_T = tidal volume during steady breathing. *Subj CND*: ⊙, V_r/V_T = 0.434; •, V_r/V_T = 1.42; ▽, V_r/V_T = 1.55. These values are indicated on horizontal scale; exhalation ceases at $1 + V_r/V_T$.

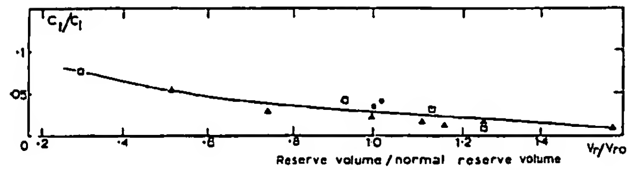

FIG. 9. Concentration (C_t), at the end of a full exhalation, after steady breathing related to reserve volume (Vr). Ci = inhaled concentration; Vr_0 = normal reserve volume of subject. ⊙, *Subj CND;* △, *subj JH;* ⊡, *subj MSR*. Each point a separate experiment.

TABLE 4. *Single-breath experiments with 0.5-μ aerosol*

Subj, Vr_0	Vr, cm³	Vt, cm³	$1-R_{600}$	R: Tidal	R: Reserve	Final Concn at End of Deep Exhalation/Inhaled Concn = C_t/Ci
CND, 835 cm	523	638	0.082	0.783	0.134	0.038
	558	630	0.093	0.769	0.137	0.037
	612	612	0.086	0.782	0.132	0.031
	1,584	702	0.032	0.840	0.125	0
	1,485	531	0.071	0.798	0.133	0
	1,021	646	0.087	0.785	0.127	0
	2,363	635	0.018	0.833	0.148	0
	1,676	592	0.044	0.799	0.157	0
	1,891	592	0.042	0.826	0.132	0
	1,106	571	0.050	0.817	0.134	0
	1,877	592	0.057	0.799	0.144	0
	1,934	613	0.028	0.831	0.141	0
	688	602	0.097	0.779	0.124	0.016
JH, 1,225 cm³	0	583	0.210	0.790	0	0.303
	0	601	0.175	0.825	0	0.423
	324	585	0.134	0.794	0.072	0.039
	1,251	612	0.085	0.809	0.106	0
	1,331	594	0.082	0.818	0.100	0
	2,322	657	0.058	0.831	0.110	0
	2,754	594	0.040	0.850	0.110	0
	1,003	612	0.073	0.832	0.099	0.0017
	172	548	0.147	0.797	0.057	0.081
	1,193	656	0.055	0.843	0.101	0
	1,802	656	0.066	0.844	0.082	0
	0	583	0.241	0.759	0	0.161
MSR 1,040 cm³	261	640	0.171	0.793	0.035	0.020
	270	649	0.142	0.815	0.042	0.021
	474	745	0.107	0.836	0.053	0.015
	568	676	0.105	0.831	0.062	0
	491	660	0.103	0.820	0.075	0.016
	441	694	0.098	0.835	0.065	0.0097
	440	668	0.096	0.816	0.086	0.010
	1,311	728	0.066	0.850	0.081	0
	1,134	618	0.055	0.855	0.090	0
	1,421	635	0.047	0.866	0.086	0
	1,541	631	0.044	0.902	0.053	0
	1,827	635	0.029	0.901	0.070	0
	1,460	690	0.058	0.850	0.090	0

reserve air. The experimental data for three observers are shown in Table 4. The frequency of breathing was near to 16 breaths/min and the corresponding rate of flow was held as nearly as possible while exhaling the aerosol. The change from air to aerosol was made without interrupting breathing. Table 4 shows the experimental recoveries in tidal and reserve air and one minus the total recovery corresponding to 600 cm³ tidal volume.

The fall of concentration during the exhalations followed a similar pattern for three observers; results of one of them,

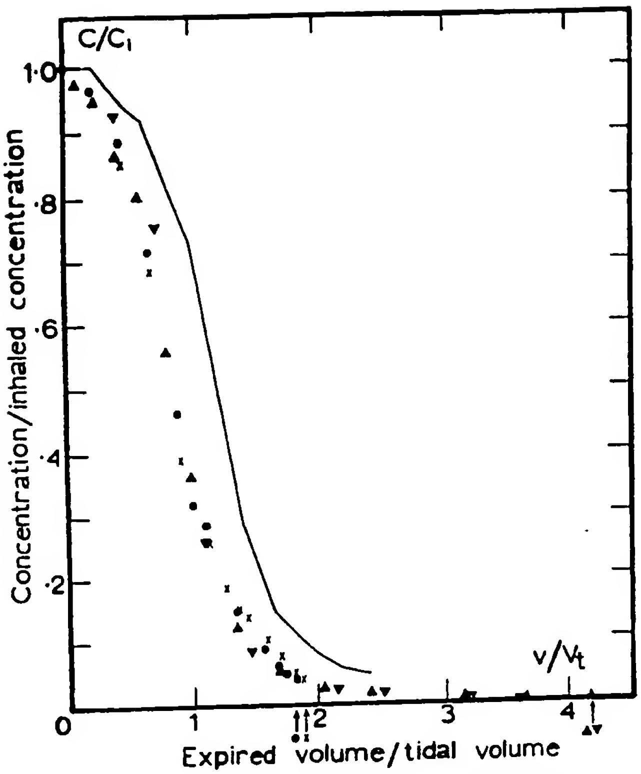

FIG. 10. Deep exhalation after a single breath of aerosol. Ci = concentration inhaled; V_T = tidal volume (about 600 cm³); C = concentration after volume V has been exhaled. *Subj CND:* ⊙, ERV 523 cm³; ×, ERV 558; △, ERV 1,877; ▽, ERV 1,934; ——— after steady breathing of aerosol, ERV = 972 cm³. End points $(1 + V_r/V_T)$ are shown on the horizontal axis.

in four experiments, are shown in Fig. 10. Two of the experiments were performed at expiratory reserve volumes about 15% less than the tidal volume and two at values over three times greater than the tidal volume. There is little dependence of the shape of the curves on the initial degree of lung expansion except at the end of the exhalation.

Also shown on Fig. 10 is deep exhalation curve taken after steady breathing of aerosol at a breathing level halfway between the limits of the single breath curves. This indicates a higher concentration of aerosol at all stages of exhalation, right from the start. Although a "plateau" is not found toward the end, as is the case for insoluble gases, there is an appreciable concentration of aerosol at the end of the reserve air. Whether or not a finite end concentration of aerosol is seen in a single-breath experiment depends on the expiratory reserve volume at which the inhalation of aerosol commenced. Arrows on the axis of abscissas (V/V_T) of Fig. 10 indicate the points $(1 + V_r/V_T)$ at which the end of the reserve air was reached in the four experiments. In the two experiments at low reserve volumes there was a finite concentration at the end of the reserve air; at high reserve volumes the end concentration was zero.

Some single-breath experiments were carried out to study the relationship between end-reserve concentration of aerosol and breathing level; three observers participated. The results are shown on Fig. 11 on which the ordinates are the ratios of the final concentration, Cf, to the inhaled concentration, Ci. It is possible to breathe at such a low level that the reserve volume is zero and the deep exhalation is equal to the tidal volume. Very high values of Cf/Ci resulted; it is not surprising that they fluctuated considerably. Relatively smooth curves were obtained for all finite values of reserve volume and the end concentration for each observer was always zero when the reserve volume was greater than his normal reserve volume (V_{r_0}), given in Table 3. The concentration ratio is plotted against V_r/V_{r_0} but the curves obtained are individual to the observer; in particular, the value of V_r/V_{r_0} above which the end concentration is zero varies from 0.55 (*subj MSR*) to 1.0 (*subj CND*).

After a period of steadily breathing aerosol, the recovery changes from 1 to 1.3 times the amount of aerosol inhaled in the last breath as $V_r - V_{r_0}$ ranges from −600 to +1,000 cm³. When only a single breath of aerosol has been taken the recovery is less and runs from about 0.9 to 0.96 over the same range. It is interesting to plot figures from these experiments as 1 − R against $V_r - V_{r_0}$, which has been done on Fig. 12. The results for three observers corrected to 600 cm³ tidal volume are shown in comparison with the deposition (1 − R) line for steady breathing (*eq 6*) of Fig. 4. The single-breath results for all observers follow a parallel course with (1 − R) about 0.03 below the steady breathing line; for $V_r - V_{r_0}$ less than −800 cm³, i.e., when the expiratory reserve volume is 200 cm³ or less, the value of 1 − R increases more rapidly, just as the steady breathing results, at very low values of the expiratory reserve volume, show deposition rising above the linear relationship of *equation 6*. The normal expiratory reserve volumes of the three subjects are indicated by arrows on the horizontal scale of Fig. 12; these positions correspond to $V_r = 0$.

The recovery of aerosol in a deep exhalation after a single breath is shown in Fig. 13 with the fractional re-

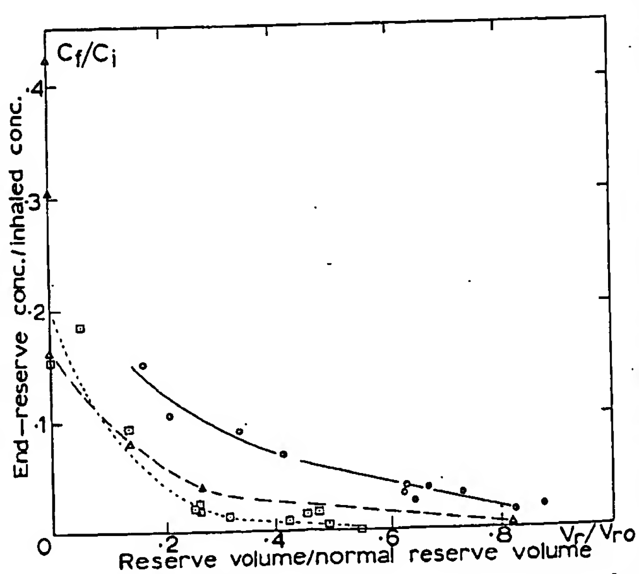

FIG. 11. Concentration (C_f) at the end of a full exhalation after inhaling a single breath of aerosol. Ci = inhaled concentration, V_r/V_{r_0} = ERV/normal ERV. C_f/Ci is always zero when $V_r/V_{r_0} >$ 1. ⊙, *Subj CND;* △, *subj JH;* ⊡, *subj MSR*. Each point is one experiment.

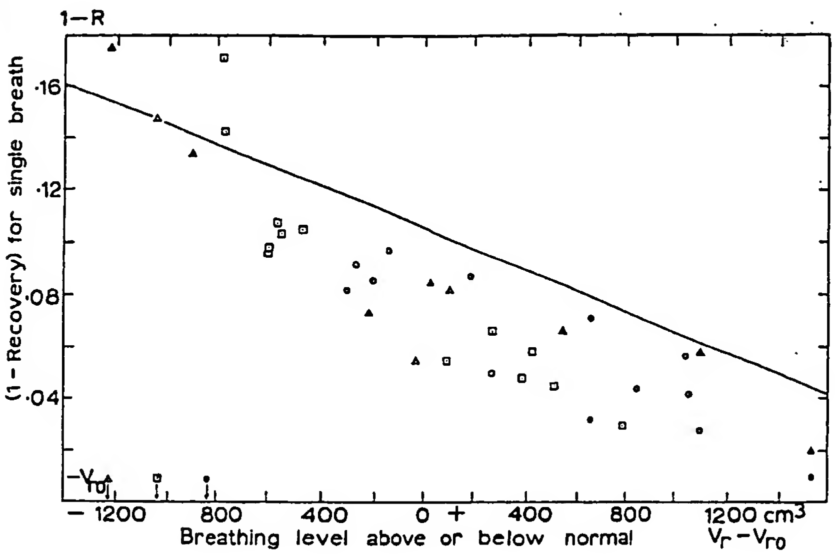

FIG. 12. "Deposition" (1 − R) from a single breath of aerosol followed by a deep exhalation. R = recovery of aerosol in tidal and reserve air. $V_r - V_{r_0} = 0$ for normal expansion of lungs. Overexpansion to right, underexpansion to left; normal ERV values for each observer shown to left at points corresponding to zero reserve volume. ⊙, *Subj CND;* △, *subj JH;* ⊡, *subj MSR;* ——— *equation 6* for steady breathing. Experimental points corrected to V_T = 600 cm³, F = 16/min. Concentration of aerosol 2-3 × 10⁶ particles/cm³.

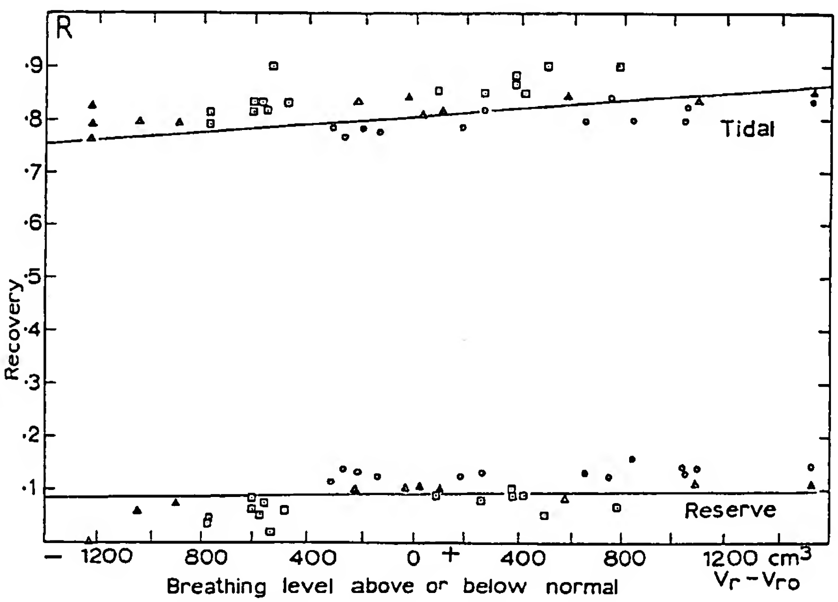

FIG. 13. Recovery (R) of aerosol from a single breath followed by a deep exhalation. Upper points give recovery in tidal volume lower points give recovery in reserve air. Recovery in reserve air tends to zero as Vr approaches zero. ⊙, *Subj CND;* △, *subj JH;* ⊡, *subj MSR.*

coveries in the tidal and reserve air plotted separately. On the average, 8 times as many particles are recovered in the tidal air as in the reserve air; both fractions increase with the reserve volume. The two straight lines drawn on Fig. 13 through the points for recovery in the tidal air and reserve air have, respectively, the equations

$$\begin{aligned} Rt &= 0.917\ (1\text{-}D) \\ Rr &= 0.113\ (1\text{-}D) \end{aligned} \qquad (12)$$

Hence

$$Rt + Rr = 1.030\ (1\text{-}D)$$

where D is given by *equation 6.* The values of Rr fall below the line and tend to zero as Vr tends to zero. Particles which are not recovered when Vr = 0 transfer from the tidal air to the residual air. As Figs. 5*B* and 7 show, particles in the reserve air can escape into the tidal air and be exhaled. Particles in the residual air, however, cannot be breathed out and must therefore deposit. The rise in deposition as Vr tends to zero, which is shown in figs. 4 and 12, is due to this. The deposition of particles in the reserve air, expressed as a fraction of the number entering the reserve air, $1 - Rr/(1 - Rt)$, is about 0.5 at the normal reserve volume and becomes unity at Vr = 0. It must be remembered that the vertical scale of Figs. 4 and 12 is magnified 5 times compared with that of Fig. 13.

It was stated by Muir (6) that all inhaled 0.5-μ particles could be recovered from a single inhalation of 500 cm³ and that the concentration at the end of the deep exhalation was zero. In fact, the present experiments show that there is always some loss of 0.5-μ particles from a single breath of 600 cm³ and that the concentration at the end of the deep exhalation is only zero if the expiratory reserve volume is sufficiently large.

Even when the concentration falls to zero at the end of the deep exhalation, i.e., when the expiratory reserve volume is sufficiently large, there is still incomplete recovery of aerosol. The explanation of this observation will be considered later.

Muir's statement has also been questioned by Altshuler (1) who obtained a recovery of 0.95 at 500 cm³ tidal volume which agrees with the present results in Fig. 12. Muir's overestimate of recovery was probably due to his overcorrecting for the instrumental dead space, as explained in Table 1 above. When 2,000 cm³ of aerosol was inhaled Muir observed a variable loss of particles. Altshuler (8) gives 0.85 recovery for this tidal volume.

CONCLUSIONS

These experiments show that lowering the expiratory reserve volume increases the loss of aerosol particles in the lungs regardless of the method of breathing. It is also evident that particles remain airborne in the reserve air during several breaths, during which time they travel up and down the alveolated airways of the lungs. Mechanical mixing between tidal and reserve air is obviously limited, since only about 10% of particles transfer during normal breathing and there is a very large gradient of aerosol concentration between the first and the last parts of the reserve air when it is exhaled. The ratio of recovery of aerosol in the tidal air to recovery in the reserve is independent of expiratory reserve volume (*eq 12*), although this has a considerable effect on deposition; it is thus evident that the mechanical mixing of tidal and reserve air is not sensitive to the degree of expansion of the lungs. This argues strongly that mixing takes place only in the dead-space airways and not in the alveolated ones.

To interpret these experimental results it is necessary to have a clear idea of the fluid mechanics of airflow in the lungs. An analysis on this basis is carried out in part II of this series of papers. In part III (5) further experimental data supporting the conclusions of part II, which accompanies this paper, are presented and a theory of particle transfer is developed which fits all the experimental conclusions and is independent of the mechanism of transfer.

C. N. Davies is the Medical Research Council Fellow of the University of Essex.

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